



Attorney Docket No. 021706-000420US

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Albert Zorko Abram, et al.

Application No.: 10/763,379

Filed: January 23, 2004

For: PHARMACEUTICAL FOAM

Customer No.: 20350

Confirmation No. 7565

Examiner: Mina Haghighatian

Technology Center/Art Unit: 1616

DECLARATION UNDER

37 C.F.R. § 1.131

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

We, the undersigned inventors, declare as follows:

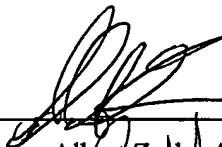
1. We are the only inventors of the invention claimed in the above-captioned patent application.
2. We understand that in an Office Action, certain of the claims have been rejected as allegedly being obvious over U.S. Patent Publication No. 2004/0043946 to Popp, which claims priority to U.S. Provisional Patent Application No. 60/407,285, filed on September 3, 2005.
3. We conceived the invention disclosed and claimed in the relevant claims of the instant application prior to September 3, 2002 and were diligent in reducing to practice the same before such date.
4. Enclosed as Exhibit A are pages 58-63 of a joint inventor's laboratory notebook, provided to illustrate our diligence in reducing the invention claimed in the above-identified application to practice. Pages 58-63 of Exhibit A demonstrate our conception and reduction to practice of a topical delivery composition in a pressurized container comprising up to 15% of a pharmaceutically active compound, about 83%-97.9% of a quick-breaking foaming agent comprised of a C₁-C₆ alcohol, a

C₁₄-C₂₂ alcohol, water, and a surfactant, and about 2%-7% of a propellant, wherein the pH adjusting agent is an acid or a base.

5. The dates on the pages of the enclosed Exhibit A have been redacted. All such redacted dates are prior to September 3, 2002.

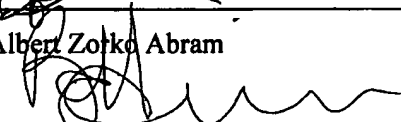
6. We further declare that all statements made herein of our knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Date: 9 August, 2005



Albert Zorko Abram

Date: 9 Aug 2005



Barry Thomas Hunt

60548902 v1



Date Redacted

E130/15

Clinda mousse - pH changesst008Aim

1. Purpose

This protocol will monitor the pH changes of clindamycin phosphate 1% foam-formulas adjusted to 5 different pHs at 25°C. The pH of the water phase and of the finished product will be monitored. The purposes of this study are to (a) redefine the correlation between pH of water phase and pH of finished product, and (b) track changes in these pH values over a 6 month period.

2. Test Materials

The base formula and variations are shown below.

Component	Grade	% w/w
Ethanol, dehydrated	USP	58.21
Stearyl alcohol	NF	0.53
Cetyl alcohol	NF	1.16
Polysorbate 60	NF	0.42
Propylene glycol	USP	2.11
Purified water	USP	to 100% (approx 36%)
Clindamycin Phosphate (804 mg/g)	USP	1.246

Potassium hydroxide 10% solution	NF	qs to required pH. 4.50, 4.55, 4.70, 4.85, 4.90
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Each can. will be filled with 19.0 +/- 0.4g water phase and 31.5 +/- 0.4g ethanol phase. Cans will be crimped and gassed with 2.66 +/- 0.25g P70.

Make a bulk ethanol phase, common to all formulations, and a bulk Clinda/water phase - divided into sub-batches for pH adjustment.

5 pHs x 8 can @ 53g/can = 2120g, plus
5 x 100 wh base = 2620g. Make enough for
3000g.

E130/15 cont'd

Date Redacted

Chuda mouse pH changes Spont.

E130/15/1 F130/15/1

Item	%	Ingredient	g/300g
1	58.21	Etanol 95 100 HG	174.6
2	0.53	Dehydrat ^{ed} water 10	15.9
3	1.16	- - 16	34.8
4	0.42	Gillet 3	12.6
5	2.11	Prop. glycol	63.3
	<u>62.43</u>		<u>187.3</u>
6	34.00	Water, pinked	102.0
7	1.246	Chuda. phosphate	37.4
	<u>35.246</u>		<u>105.7</u>
Total	97.676		

KOH 10% 9.3 to pHWater \rightarrow 100%

Slightly less water is being used at Item 6 to allow for variable KOH addition. Then make up to full weight with water.

From previous studies (E123/24, p. 148) the amount of 1% KOH used was 1 - 2g per 10g of water phase.

Water phase divided into lots of 210g. Full weight of water phase (incl. KOH) is $(100 - 62.43) = 37.57$ x 30 = 1127g. + 5 = 225g. So each lot of 210g is adjusted to pH with 10% KOH then made up to 225g with water.

E120/15 can

Date Redacted

Soltec Research Pty Ltd. Manufacturing Batch Record
(Samples: only)

Product Name: **SP008** Clindamycin Phosphate Mousse
pH testing

Formulation No: F130/15
Batch No: **E130/15**
Date: **2020-09-20**

Batch Size: **3000** grams

Item No.	% w/w	Ingredient	Lot #	Theoretical Mass Weighed.	Actual Mass weighed	Weighted By	Checked By
1	58.21	Ethanol 100HG	21280	1748.300	1751.1g	884	884
2	0.42	Crillet 3	13347	12.600	12.77	884	884
3	0.53	Dehydtag wax 18	13347	15.900	15.89	884	884
4	1.16	Dehydtag wax 18	13347	34.800	34.83	884	884
5	2.11	Propylene glycol	21097	63.300	63.62	884	884
6	34.00	Purified water	—	1020.000	1020.33	884	884
7	1.25	Clindamycin phosphate	20086	37.380	37.30	884	884
8	qs	Potassium hydroxide 10% soln					
9	qs	Purified water					
		TOTAL		2930.280			

1872.9
615.6
2488.5
Actual = 2497.5
37.46
1403.46
414.13
1020.33

(No propellant)

Method:
Ethanol phase:
Dissolve 2-5 in ethanol.
Water phase:
Add 7 to 6 and mix till dissolved
Prepare a 10%w/w KOH solution and adjust water phase as reqd.
Add remaining purified water to 100%.

Fill weights: (50.5g base)
Ethanol ph 31.5 +/- 0.40g
Water ph 19.0 +/- 0.40g
Propellant 2.88 +/- 0.25g

Date Redacted

E130/15 contd

Date Redacted

Chloro mouse pH SP 008

Take 211 g \pm 1 g of water phase, and add 10% KOH soln (10% w/w 20045 in water) to achieve pH, \pm 0.01 unit. Then \rightarrow 225 g \pm 1 g + re-check pH

pH meter calibrated at $25^\circ \pm 2^\circ\text{C}$, sample solution at $25^\circ \pm 2^\circ\text{C}$.

19.0 \pm 0.4 g of ^{soln} water phase into 7 aerosol can (35 x 125 mm Exal), add 31.5 \pm 0.4 g of ethanol phase, then cimp. Gas with 2.65 \pm 0.25 g. Remaining water phase into 120 ml glass jar. All samples stored at 25°C . 1 sample of water phase + ethanol phase for pH measurement (not aerosol).

g 10% KOH soln	Req. no.	pH nominal	pH actual	App. pH base
0.41 g	E130/15/2	4.50	4.49	
0.46 g	- 3	4.55	4.57	
0.56 g	- 4	4.70	4.70	
0.78 g	- 5	4.85	4.85	
0.82 g	- 6	4.90	4.90	

re-checked pH 4.0 buffer after each addition, batch. (Initial pH 3.21)

For 2nd batch aerosol, the water was added to 224 g immediately (because such a small amt of KOH is reqd)

Checked both pH 4 & 7 at end - both within 0.02

Recalibrate pH meter at 40°C & check pH of the 5 mixed aq/eth phases at 40°C

E130/15 contd

Date Redacted

date

App. pH @ 25°C

E130/15/2

4.85

3

4.92

pH 4 now = 3.99

4

5.03

5

5.15

6

5.20

pH 4 now = 4.00

pH 7 now = 7.02

Date Redacted

The above jars placed at 25°C on 30/10.
Cans filled yesterday were gassed today with
2.66 to 2.5% P₂O₅.

Cans waterbatted, labelled & weighed. Weights
are to check in gas loss - not for formal study.

into 25°C today.

sample 7 label used

For Laboratory Evaluation Only
Not for Human Use

Clindamycin Mouse pH testing SP008

Time point: 1 2 4 weeks 2 3 6 months

Storage temperature: 25°C

E130/15/8

SOLTEC RESEARCH Pty. Ltd.

Date Redacted

BEST AVAILABLE COPY

E130/15 contd

Date Redacted

Chlor S8008 - 1 week

(Actually 8 days)

Check pH of the 5 jars from
25°C.

E130/15/1	8.6	4.43
5	4.54	
4	4.66	
3	4.81	
6	4.87	

pH 4 new = 3.98, adj. → 4.00

Recal. @ 45°C

App pH @ 45°C =

2	4.84
3	4.91
4	5.03
5	5.16
6	5.21

pH new = 3.99, adj. → 4.00

pH 4 new = 4.00



Date
Redacted

to p70